Original Research Article

Post-Intubation Airway Related Adverse Effects: A Comparison between Intra-Cuff Dexamethasone and Intra-Cuff Alkalinized Lignocaine

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Abstract

Post-intubation airway related adverse effects such as coughing on the endotracheal tube (ETT), restlessness, hoarseness and sore throat are common and undesirable outcomes of anaesthesia using endotracheal intubation. This prospective randomized single blind study was carried out to compare the effectiveness of intra-cuff dexamethasone and alkalinized lignocaine in reducing the incidence of post-intubation airway related adverse effects. Eighty four patients aged 18 – 60 years, of ASA status I or II, were randomly allocated into three groups: air, dexamethasone and alkalinized lignocaine. Their ETT cuffs were inflated according to the group they were allocated to. The incidence of coughing on the ETT, restlessness, hoarseness and sore throat was assessed, postoperatively. The results showed a significant difference in the incidence of cough, restlessness, hoarseness and sore throat in the dexamethasone group compared to the air group. All the patients had minimal or no sore throat at all documented times. Both intra-cuff dexamethasone and alkalinized lignocaine significantly reduced the incidence of hoarseness. However, alkalinized lignocaine additionally lowered the incidence of restlessness, significantly.

Keywords: Post-intubation, adverse effects, endotracheal, dexamethasone, lignocaine

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Introduction

Endotracheal intubation is the definitive method of securing the airway during general anaesthesia. It facilitates positive pressure ventilation and confers protection of the airway from aspiration of gastric content. However, endotracheal intubation has been known to cause post-intubation airway related adverse effects, which include post-operative coughing on the tube, restlessness, hoarseness and sore throat. The latter, although regarded as a minor complication, is often distressing for the patient and remains as an unpleasant post-operative memory. The incidence of sore throat ranges from 14.4 to 50% (1). Post-intubation airway related adverse effects may result in laryngospasm, tachycardia, hypertension, cardiac ischemia, bleeding, increased intracranial and intraocular pressures which may impose serious implications on patients, thus the importance in preventing its occurrence (2).

It was postulated that post-intubation airway related adverse effects were due to irritation and inflammation of the airway, which may occur during intubation, as insertion of an endotracheal tube (ETT) may irritate or damage the mucosal tissue, causing oedema and inflammation (3). The risks are increased if intubation was particularly difficult or traumatic. It has also been proposed that the incidence and severity of sore throat post-intubation is highly correlated to the endotracheal cuff design, in particular the cuff-trachea contact area (4). Low-pressure high-volume cuffs cause a larger area of trachea mucosal erosion compared to high-pressure low-volume cuffs (5). Over-inflation of ETT cuffs, resulting in high cuff pressures, has also been associated with trachea mucosal damage, and exacerbation of post-intubation airway related adverse effects (6). Cuff pressures above 39 cm H_2O are shown to reduce trachea mucosal microcirculation (7). As a cuffed ETT is inevitable

in certain cases, the potential airway irritation and inflammation associated with its use may be minimized by ensuring a swift and smooth intubation, and monitoring intra-cuff pressure.

Alkalinized lignocaine (lignocaine hydrochloride in 8.4% sodium bicarbonate) administered intra-cuff has repeatedly been shown to reduce the incidence of post-intubation airway related adverse effects (8,9). Lignocaine exerts its local anaesthetic action by inhibiting the ionic fluxes needed for the initiation and conduction of impulses, thus stabilizing the neuronal membrane (10). It also limits the potential damage to the tracheal mucosa by suppressing 'bucking' on the ETT (8). Sodium bicarbonate on the other hand alkalinizes lignocaine hydrochloride and increases its diffusing capacity through the hydrophobic ETT cuff membrane (9). However, as lignocaine hydrochloride does not possess any anti-inflammatory action, its exact mechanism in preventing post-operative sore throat is still unknown (11).

Corticosteroids are known for their anti-inflammatory actions. Their mechanism of action is thought to be by inducing lipocortins which are phospholipase A2 inhibitory proteins. These proteins are thought to be responsible in inhibiting the release of arachidonic acid, the common precursor of potent mediators of inflammation, such as prostaglandins and leukotrienes (12). By reducing or inhibiting the inflammatory response, it should be possible to reduce the incidence of post-operative cough, restlessness, hoarseness and sore throat. Studies using topically applied steroid, intravenous dexamethasone and inhaled fluticasone propionate have shown favourable results in reducing post-operative sore throat (3,11,13,14). Based on the above studies using steroids, we postulate that intra-cuff dexamethasone may reduce the incidence of post-intubation airway related adverse effects by its diffusion through the ETT cuff and subsequent anti-inflammatory action on the tracheal mucosa. The objective of this study was to compare the effectiveness of intra-cuff dexamethasone versus alkalinized lignocaine with intra-cuff air as a control group, in reducing post-intubation airway related adverse effects.

Materials and Methods

This was a prospective randomized, single-blind controlled study. Following institutional ethics approval, 90 patients were recruited. Patients were aged between 18 and 60 years, with American Society of Anaesthesiologists (ASA) status class I or II, scheduled for surgery lasting between 30 to 360 mins, under general anaesthesia with endotracheal intubation. Exclusion criteria were those undergoing surgery of the oral cavity and pharynx, with anticipated difficult airway, requiring the use of nasogastric tubes and throat packs, with pre-existing upper respiratory tract infections, sore throat, hoarseness and those on steroid therapy.

Pre-anaesthetic assessments of the patients were done a day prior to their surgery. The study protocol was explained and written informed consent taken. Using computer generated randomised numbers, patients were randomized into one of three groups; air, dexamethasone or alkalinized lignocaine group. Patients were premedicated with oral midazolam 7.5 mg upon call to the operating theatre (OT). In the OT, standard monitoring included non-invasive blood pressure monitoring, pulse oximetry, electrocardiogram and capnograph. After intravenous (IV) access was obtained, the patient was pre-oxygenated with 100% oxygen for three minutes, followed by IV induction with fentanyl 2 mcg/kg, propofol 2 mg/kg and rocuronium 0.6 mg/kg. Single use polyvinyl chloride ETTs (Portex® Profile tracheal tube) with low-pressure-high-volume cuffs, of inner diameter size 7.0-7.5 mm for females and 8.0-8.5 mm for males were used. The ETT was lubricated with sterile water and intubations performed by anaesthetic doctors with at least one year of experience in anaesthesia. Direct laryngoscopy was performed using either a Macintosh 3 or 4 laryngoscope blade followed by intubation. The ETT cuff was inflated according to the randomised protocol. The ETT cuffs in the air, dexamethasone and lignocaine groups were inflated with air, 2 ml (8 mg) of dexamethasone, or 2 ml (2%) lignocaine respectively. An additional 2-3 ml of saline or 8.4% sodium bicarbonate was added into the dexamethasone and alkalinized lignocaine groups respectively, till no leak was audible at an intra-airway pressure of 20cm H_2O. The initial cuff pressure was measured and recorded with a Mallinckrodt cuff pressure gauge (Mallinckrodt Medical, Athlone, Ireland). Patients who had intubation unsuccessful on the first attempt, were excluded. Anaesthesia was then maintained with a 50% oxygen-air mixture and sevoflurane, titrated to achieve a MAC of 1-1.3. Neuromuscular blockade was monitored and additional rocuronium doses given to maintain a train-of-four (TOF) count of zero.

At the end of the surgery, the cuff pressure was again measured and recorded. Sevoflurane was discontinued, 100% oxygen was administered and residual neuromuscular blockade antagonized with atropine 0.02 mg/kg and neostigmine 0.05 mg/kg when at least 3 train-of-four twitches were present. Oral suctioning was done with care under direct vision just before extubation. Upon fulfilling extubation criteria (TOF ratio at least 90%, regular spontaneous ventilation present and able to follow verbal commands) the patient was extubated and

100% oxygen was administered via face mask. The patient was assessed by the attending anaesthetist for coughing on the ETT, restlessness before extubation and hoarseness in the recovery area before discharge. The severity of post-extubation sore throat was evaluated with the visual analogue score scale (VAS, 0-100 mm) at 30 minutes, in the recovery room, and at 2 and 24 hours in the ward. Based on previous studies', sample size was calculated using nQuery Advisor version 6.01 Software (2,4), 25 patients were required in each group to permit a type I error of $\alpha = 0.05$, type II error of $\beta = 0.05$ and power of 95%. Considering a drop-out rate of 20%, 30 patients were required in each group. Statistical analysis was performed using SPSS Statistic version 17.0. Data was tested using analysis of variance (ANOVA) and non-parametric test was used to assess cough, restlessness, hoarseness and sore throat. A p value < 0.05 was considered statistically significant.

Results

Ninety patients were enrolled in this study. However, six patients were excluded, of which four required more than one intubation attempt and two patients had surgery exceeding six hours. The patients' demographic and perioperative details were comparable between groups (Table1).

The volume of intra-cuff media required to prevent leak around the ETT in the air group was more but not statistically significant. Between the dexamethasone and lignocaine hydrochloride groups, intra-cuff volumes were comparable. There were no significant changes from the initial volumes of the intra-cuff media in all three groups at the end of anaesthesia. The pressure required to prevent leak around the ETT in all three groups were comparable. There were no significant changes from the initial cuff pressures in all three groups at the end of the anaesthesia (Table2).

Comparing the three groups, the incidence of coughing on the ETT was less but not statistically significant in the dexamethasone and alkalinized lignocaine groups compared to the air group. The incidence of restlessness was lower in the dexamethasone and alkalinized lignocaine groups, but only statistically significant in the alkalinized lignocaine group. The incidence of hoarseness was also lower in the dexamethasone and alkalinized lignocaine groups compared to the air group, and this was statistically significant. However, between the dexamethasone and lignocaine hydrochloride groups, the incidence of coughing, restlessness and hoarseness was comparable (Table3).

The mean VAS scores for sore throat in the dexamethasone and alkalinized lignocaine groups were lower compared to the air group but this was statistically significant only at 2 and 24 hour scores, in the ward. Between the dexamethasone and lignocaine hydrochloride groups, the mean VAS scores were comparable at all documented times (Table 4).

Discussion

The over-inflation of ETT cuffs with high intra-cuff volumes, either at initial cuff inflation post-intubation and/or at the end of surgery results in high intra-cuff pressures which may result in undesirable airway adverse events. The present study showed insignificant changes from the initial pressure and volume of the ETT cuffs, at the end of anaesthesia. This was in contrast to Shroff and Patil's (2009) and Combes' et al. (2001) where statistically significant increments in intra-cuff pressures were observed in the air group (2,6). This may be due to the fact that in this study, anaesthesia was maintained with an oxygen air mixture, whereas in the mentioned prior studies, an oxygen and nitrous oxide mixture was used. In the blood, nitrous oxide is 34 times more soluble than nitrogen. The diffusion of nitrous oxide into the cuff is facilitated by the blood/gas solubility coefficient of 0.468/0.013 for nitrous oxide/nitrogen. The cuff pressure is increased as nitrous oxide diffuses into the air filled cuff more quickly than it leaves the cuff (2).

This study also showed that higher volumes and pressures were required to prevent any leak around the ETT when air was used as the inflation media as compared to liquid, such as dexamethasone and alkalinized lignocaine. Shroff and Patil (2009) and Estebe et al. (2002 & 2005) in their studies demonstrated that intra-cuff alkalinized lignocaine and saline significantly reduced the incidence of post-intubation airway related adverse effects compared to air. This was possibly due to the intra-operative accumulation of intra-cuff nitrous oxide in the air group which was evident at the end of anaesthesia (2,8,9). Inflating the ETT cuffs with liquids obliterates air pockets in the ETT cuffs and confers added benefit by preventing excessive intra-cuff pressures (9).

The incidence of coughing in our study was lower but not statistically significant in the dexamethasone and alkalinized lignocaine groups. The incidence of coughing in the air group was higher in the studies done by Estebe et al. (2002 & 2005) (70% and 96%), as compared to our study (43%). This could be explained by their usage of nitrous oxide, thus the resultant higher intra-cuff pressure at the end of anaesthesia (8,9). In the same study, intra-cuff alkalinized lignocaine reduced the incidence of coughing by 56%-65% compared to air group (8,9).

Table 1: Demographic and perioperative data. Data are presented as mean SD or number (%) as appropriate.

Variables	Air (n = 28)	Dexamethasone (n = 28)	Alkalinized lignocaine (n = 28)
Age (year)	44 ± 12	41 ±13	47±10
Sex (Male /Female)	15 / 13	17 /11	15 /13
Weight (kg)	66 ± 10	65 ± 10	66 ± 10
Height (cm)	166 ± 7	165 ± 8	167 ± 6
Duration of anaesthesia (minute)	126 ± 77	124 ± 81	103 ± 63
Smoker	8 (28%)	10 (35%)	10 (35%)

Table 2: Volume of intra-cuff media and intra-cuff pressure at the start and end of anaesthesia.Data are presented as mean ± SD.

Volume and Pressure	Air (n = 28)	Dexamethasone (n = 28)	Alkalinized lignocaine (n = 28)
Volume: Start of anaesthesia (ml)	7.3 ± 0.7	4.9 ± 0.5	4.8 ±0.5
End of anaesthesia (ml)	7.2 ± 0.8	4.8 ± 0.5	4.7 ± 0.6
Pressure: Start of anaesthesia (cm H_2O)	26.0 ±1.0	23.0 ± 0.9	24.0 ± 1.1
End of anaesthesia (cm H_2O)	25.0 ±1.0	23.0 ± 1.1	23.0 ± 1.0

Table 3: Incidence of cough, restlessness and hoarseness at emergence. Data are presented as number (%)

Variables	Air	Dexamethasone	Alkalinized lignocaine
Cough	20 (43.5)	14 (30.4)	12 (26.1)
Restlessness	8 (72.7)	2 (18.2)$^{+}$	1 (9.1)$^{\#+}$
Hoarseness	7 (77.8)	1 (11.1)$^{*+}$	1 (11.1)$^{\#+}$

*$p < 0.05$ between group air vs dexamethasone
#$p < 0.05$ between group air vs alkalinized lignocaine
+ with Yates' correction

Table 4: Visual analog scale (VAS) score for sore throat at different time intervals. Data are presented as mean ± SD.

Time Interval	Air (n = 28)	Dexamethasone (n = 28)	Alkalinized lignocaine (n = 28)
30 minutes	11 ± 13	4 ± 8	3 ± 7
2 hours	8 ± 10	0 ± 1*	1 ± 4$^{\#}$
24 hours	1 ± 4	0*	0$^{\#}$

*p < 0.05 between group air vs dexamethasone

#p < 0.05 between group air vs alkalinized lignocaine

In our study, alkalinized lignocaine reduced the incidence of coughing by 40% compared to air group. In Shroff and Patil's (2009) study, the incidence of restlessness was 72% and 20%; and hoarseness 78% and 32%, in the air and alkalinized lignocaine groups respectively (2). The incidence of restlessness and hoarseness was significantly lower in the alkalinized lignocaine groups in Shroff and Patil's and our study (2). The incidence of restlessness and hoarseness in our study was also lower in dexamethasone group compared to air group, although only hoarseness was significantly reduced.

The incidence of sore throat in the air group in this study was 43% which was comparable to that found in a study by Biro et al. (2005) (1). There was minimal or no complain of sore throat in the

dexamethasone and alkalinized lignocaine groups at 2 and 24 hours post-operatively, and this was statistically significant compared to the air group. The intensity of sore throat for all three groups in this study was mild and similar to that reported by Estebe et al. (2005) (9). The ability of lignocaine to diffuse out of ETT cuffs was first described by Sconzo et al. (1990) (15). Estebe et al. (2002) showed increased diffusion of lignocaine when it was alkalinized and plasma lignocaine level was detected in the venous blood samples of patients who had their ETT cuff inflated with alkalinized lignocaine. Lignocaine diffusion was possible as the ETT cuff is semi-permeable, thus making it a potential drug reservoir (8).

Ayoub et al. (1998) showed that topical application of betamethasone over the ETT reduced the incidence of cough, hoarseness and sore throat post-operatively (3). Park et al. (2008) administered prophylactic intravenous dexamethasone with double lumen intubation and found a decrease in the incidence and severity of sore throat and hoarseness post extubation (13). Tazeh-kand et al. (2010) found that inhaled fluticasone propionate given pre-induction decreased the incidence and severity of post-operative cough, sore throat and hoarseness (14). Steroids with their anti-inflammatory action has been attributed to these outcomes (11,13,14). In this study it could be possible that dexamethasone diffused through the ETT cuff, acting on the tracheal mucosa in contact with it, thus reducing the inflammatory process occurring in the tracheal mucosa. Measurement and detection of dexamethasone levels in venous blood samples of patients who had their ETTs inflated with dexamethasone might have confirmed this. Alkalinized lignocaine on the other hand diffuses through and anaesthetizes the tracheal mucosa in contact with the cuff, and reduces the firing of their irritant receptors (14). These two mechanisms are most probably responsible for the observed reduction in the incidence of coughing on the ETT, restlessness, hoarseness, and sore throat in the postoperative period. In conclusion, both intra-cuff dexamethasone and alkalinized lignocaine significantly reduced the incidence of hoarseness, however alkalinized lignocaine additionally lowered the incidence of restlessness significantly. All the patients had minimal or no sore throat at all documented times.

References

1. Biro P, Seifert B, Pasch T. Complaints of sore throat after tracheal intubation: a prospective evaluation. Eur J Anaesthesiol 2005;22(4):307-311.
2. Shroff P, Patil V. Efficacy of cuff inflation media to prevent postintubation-related emergence phenomena: air, saline and alkalinized lignocaine. Eur J Anaesthesiol 2009;26(6):458-462.
3. Ayoub MC, Ghobashy A, McGrimely L, et al. Wide spread application of topical steroids to decrease sore throat, hoarseness and cough after tracheal intubation. Anesth Analg 1998;87(3):714-716.
4. McHardy FE, Chung F. Postoperative sore throat: cause, prevention and treatment. Anaesthesia 1999;54(5):444-453.
5. Mandoe H, Nikolajsen L, Lintrup U, Jepsen D, Moolgaard J. Sore throat after endotracheal intubation. Anesth Analg 1992;74(6):897-900.
6. Combes X, Schauvliege F, Peyrouset O, et al. Intracuff pressure and tracheal morbidity: influence of filling with saline during nitrous oxide anesthesia. Anesthesiology 2001;95(5):1120-1124.
7. Loeser EA, Hodges M, Gliedman J, Stanley TH, Johansen RK, Yonetani D. Tracheal pathology following short term intubation with low and high pressure endotracheal tube cuffs. Anesth Analg 1978;57(5):577-579.
8. Estebe JP, Dollo G, Le Corre P, et al. Alkalinization of intracufflidocaine improves endotracheal tube-induced emergence phenomena. Anesth Analg 2002;94(1):227-230.
9. Estebe JP, Gentili M, Le Corre P, Dollo G, Chevanne F, Ecoffey C.Alkalinization of intracufflidocaine: efficacy and safety. Anesth Analg 2005;101(5):1536-1541.
10. Stoelting RK, Hillier SC. Pharmacology & Physiology in Anesthetic Practice. 4th ed - Local anesthetics. Philadelphia: Lippincott Williams & Wilkins, 2006, pp-181-182.
11. Sumathi PA, Shenoy T, Ambareesha M, Krishna HM. Controlled comparison between betamethasone gel and lidocaine jelly applied over tracheal tube to reduce postoperative sore throat, cough, and hoarseness of voice. Br J Anaesth 2008;100(2):215-218.
12. Stoelting RK, Hillier SC. Pharmacology & Physiology in Anesthetic Practice.4th ed.- Hormones and Drugs. Philadelphia: Lippincott Williams & Wilkins, 2006, pp-461-465.

13. Park SH, Han SH, Do SH, Kim JW, Rhee KY, Kim JH. Prophylactic dexamethasone decreases the incidence of sore throat and hoarseness after tracheal extubation with a double-lumen endobronchial tube. Anesth Analg 2008;107(6):1814-1818.

14. Tazeh-kand NF, Eslami B, Mohammadian K. Inhaled fluticasone propionate reduces postoperative sore throat, cough and hoarseness. Anesth Analg 2010;111(4):895-889.

15. SconzoJM, Moscicki JC, Difazio CA. In vitro diffusion of lidocaine across endotracheal tube cuffs. Reg Anesth 1990;15(1):37-40.